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BIOCHEMISTRY

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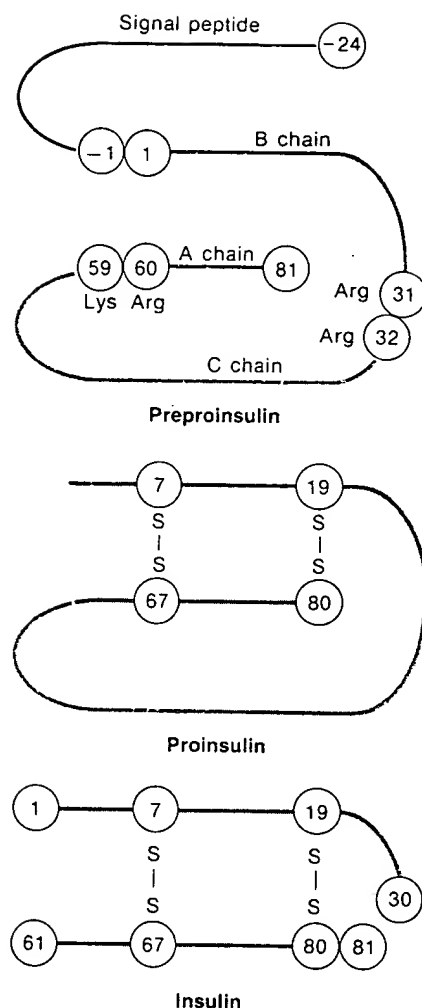


Figure 29-10

Biosynthesis of insulin. Insulin is synthesized by membrane-bound polysomes in the β cells of the pancreas. The primary translation product is preproinsulin, which contains a 24-residue signal peptide preceding the 81-residue proinsulin molecule. The signal peptide is removed by signal peptidase, cutting between Ala (-1) and Phe (+1), as the nascent chain is transported into the endoplasmic reticulum. Proinsulin folds and two disulfide bonds cross-link the ends of the molecule as shown. Before secretion, a trypsin-like enzyme cleaves after a pair of basic residues 31, 32 and 59, 60; then a carboxypeptidase B-like enzyme removes these basic residues to generate the mature form of insulin.

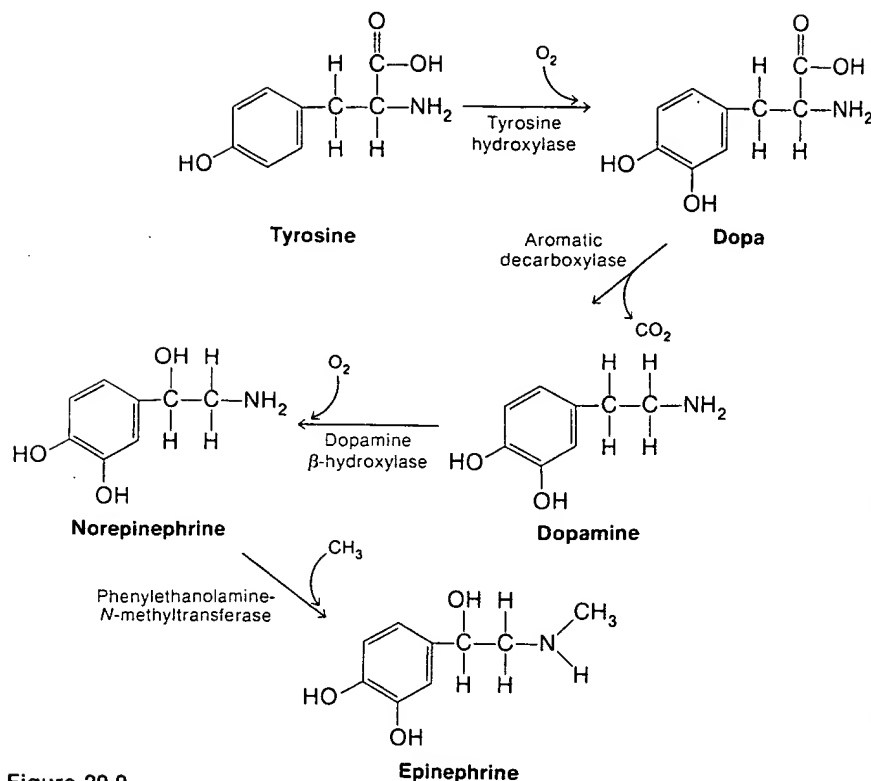


Figure 29-9

Pathway of catecholamine synthesis.

tyrosine to 3,4-dihydroxyphenylalanine (dopa), is catalyzed by tyrosine hydroxylase. This is the rate-limiting enzyme in the pathway, and its activity is controlled by a cAMP-dependent protein kinase. Epinephrine and norepinephrine are stored in chromaffin granules. These granules contain catecholamine and ATP in a molar ratio of 4:1 complexed with protein. Neural stimulation of the medulla is mediated by acetylcholine, which binds to receptors on the membranes of chromaffin cells and leads to a local depolarization and an influx of Ca^{2+} , and this results in the fusion of some chromaffin granules with the cell membrane and, consequently, extrusion of a packet of catecholamines and ATP into the circulation.

Polypeptide Hormones Are Synthesized as Precursors

All polypeptide hormones for which the mechanism of synthesis is known are synthesized as precursors. The primary translation products of the mRNAs coding for insulin, glucagon, prolactin, growth hormone, gastrin, parathyroid hormone, vasopressin, and corticotropin have been characterized by cell-free translation, and in many cases, the mRNAs that code for these hormones have been cloned into bacterial plasmids and sequenced. In all these cases, the primary translation product contains 20 to 30 predominantly hydrophobic amino acid residues at the amino terminus that